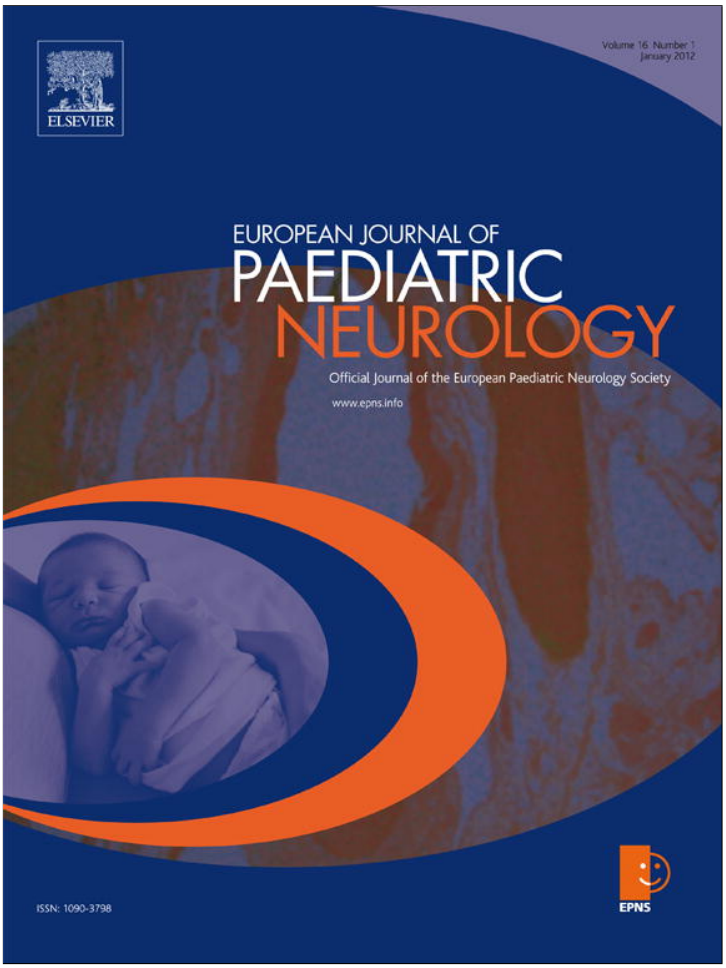

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Original article

Epilepsy and cerebral palsy: Characteristics and trends in children born in 1976–1998

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ABSTRACT

Background: Although epilepsy is common in children with cerebral palsy (CP), no data exists on prevalence rates of CP and epilepsy.
Aims: To describe epilepsy in children with CP, and to examine the association between epilepsy and neonatal characteristics, associated impairments and CP subtypes.
Methods: Data on 9654 children with CP born between 1976 and 1998 and registered in 17 European registers belonging to the SCPE network (Surveillance of Cerebral Palsy in Europe) were analyzed.
Results: A total of 3424 (35%) children had a history of epilepsy. Among them, seventy-two percent were on medication at time of registration. Epilepsy was more frequent in children with a dyskinetic or bilateral spastic type and with other associated impairments. The prevalence of CP with epilepsy was 0.69 (99% CI, 0.66–0.72) per 1000 live births and followed a quadratic trend with an increase from 1976 to 1983 and a decrease afterwards. Neonatal characteristics independently associated with epilepsy were the presence of a brain malformation or a syndrome, a term or moderately preterm birth compared with a very premature birth, and signs of perinatal distress including neonatal seizures, neonatal ventilation and admission to a neonatal care unit.
Conclusions: The prevalence of CP with epilepsy followed a quadratic trend in 1976–1998 and mirrored that of the prevalence of CP during this period. The observed relationship between epilepsy and associated impairments was expected; however it requires longitudinal studies to be better understood.

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1. Introduction

Epilepsy is common in children with cerebral palsy (CP) and has been used as a marker of severity in this disorder.[1] It is estimated to affect between 15 and 60% of children with CP.[1–3] Epilepsy is associated with greater impairment of cognitive function,[4] with lower probability of walking[5], with more severe behavioural problems,[6,7] a poorer quality of life in compromising autonomy[8] and inevitably a greater burden of care.

Over the last decade, several studies have described epilepsy in children with CP.[9–13] Compared with children suffering from epilepsy alone, epilepsy in children with CP is characterised by an earlier age of onset, a lower frequency of generalized seizure, a greater need for polytherapy and second-line anti-epileptic drugs, and with lower probability of remaining seizure-free.[2,10] However, most of the studies were hospital-based increasing the possibility of selection bias[9–13] and all but three[10,11,14] studied less than two hundred children. Furthermore, there are limited data on both trends in prevalence of CP and epilepsy, and trends in frequency of epilepsy among children with CP.

The Surveillance of Cerebral Palsy in Europe (SCPE) network comprises a large population-based database of children with CP. The objectives of this study were to describe trends in the prevalence of children with CP and epilepsy born between 1976 and 1998, and to examine the association between epilepsy and neonatal characteristics, associated impairments and CP subtype, using the SCPE database.

2. Methods

2.1. Study population

Data were collated from the SCPE database which has been described previously.[15,16] Children with CP were included if they were born between 1976 and 1998. Children from the Tübingen survey (Germany) were excluded as this survey only recorded bilateral spastic CP cases. Children from the Mersey register (United Kingdom) were excluded as information on epilepsy was missing for 91% of children. All other children with missing information for epilepsy were also excluded (Fig. 1). To calculate prevalence rates per 1000 live births, we selected children whose mother lived in an area covered by the survey or register at the time of birth. The exceptions were the two French registers with known migration patterns, where cases were defined as living in the area at the time of registration. Cases from the two registers without any denominator available could not be included in the analysis of prevalence rates.

2.2. Characteristics of the children

Epilepsy was defined as a history of two unprovoked seizures after the neonatal period, (i.e. after 28th day of birth), but before CP registration.[17] Febrile seizures were excluded. Epilepsy was considered active if the child was on medication at time of registration. The way the information on diagnosis of epilepsy was obtained depended on the ascertainment method of the register. Indeed, SCPE is a network of registers with different ascertainment methods. In several registers, data are abstracted from medical records (in which the word epilepsy and/or seizures and/or names of anti-epileptic treatment are present), in other registries, it is the paediatrician in charge of the child who confirms the diagnosis of epilepsy and provides information directly to the register, using a data collection proforma.

CP of postneonatal origin was defined by the presence of a specific event or episode that happened after 28 days of age. Gestational age was categorized as term (≥37 weeks), moderate preterm (32–36 weeks) or very premature birth (<32 weeks). Brain malformation was defined as an antenatal developmental abnormality of the brain and coded according to the 9th version of International Classification of Diseases. Syndromes were defined in accordance with Smith's Recognisable Patterns of Human Malformation, 5th Revised Edition.[18] Other neonatal characteristics used in this study were: admission to a neonatal care unit (NCU), ventilation

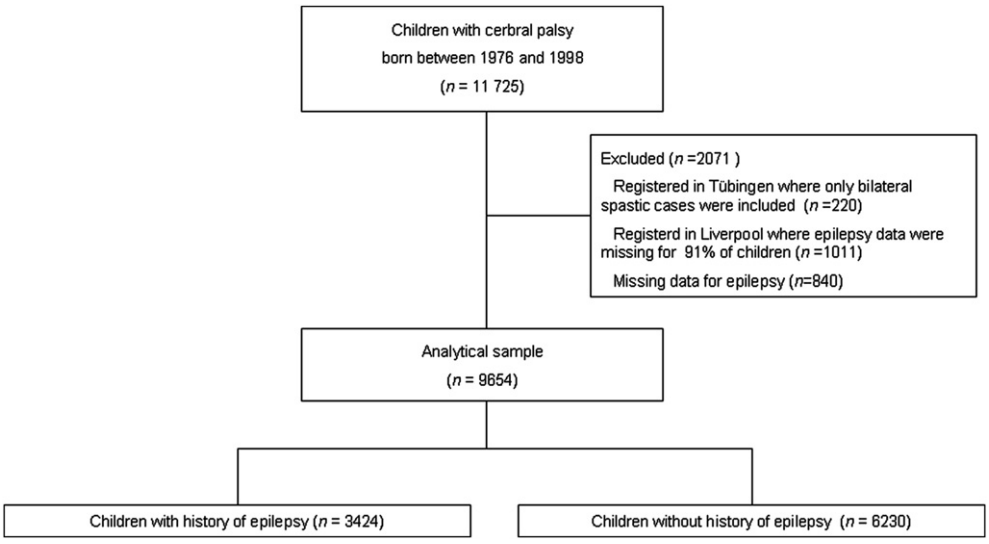

Fig. 1 – Selection of children with cerebral palsy and epilepsy.

during hospitalization in the NCU, apgar score recorded at 5 min and presence of neonatal seizures, defined as convulsions within the first 72 h of life, excluding febrile convulsions. For each child, a Z score for birthweight by gestational age was derived, using Marsal fetal growth standard curves for Swedish children,[19] and Gardosi fetal growth standard curves for other children.[20] Small for gestational age was defined as a Z score of less than −2.

CP subtypes included spastic bilateral (BS), spastic unilateral (US), dyskinetic and ataxic. Severity of the gross motor function was categorized as independently walking, walking with aids, or unable to walk. Members of SCPE agreed to use the standardized GMFCS for children born from 1997 onward. Consequently, data on GMFCS could not be used in the present study. Severe intellectual impairment was defined as IQ below 50; severe visual impairment as visual acuity of less than 6/60 (Snellen scale) or 0.1 (Decimal scale) in the better eye following correction and severe hearing impairment as a loss of more than 70 dB in the better ear, before correction.

2.3. *Statistical analysis*

Poisson regression was used to investigate trends in prevalence of CP. To take account of the fact that data were provided by different registers covering different time periods (Table 1), initially the within register trends were analyzed, with a linear term for individual birth year. Non-linearity of the trend using polynomial terms for birth years was tested up to the third order. Subsequently pooled data was used to investigate trends across registers. The initial model contained only individual birth years; the addition of a term for register allowed for testing of a register effect. Adding an interaction term between register and birth year provided a test for variation in trends between registers. Likelihood-ratio Chi squared tests were used to compare nested models.

Categorical variables are summarised as frequencies and percentages and continuous variables as median and interquartile range (IQR, 25th and 75th percentiles). To test for the association between epilepsy and neonatal characteristics or associated impairments, chi-square test or chi-square test for trend were used for univariate analyses. For each characteristic, the odds ratio (OR) of epilepsy and associated 95% confidence interval (CI) are presented. The characteristics were entered into a full multilevel logistic regression model, taking into account the clustering of children among registers. A parsimonious model was then developed, using a backward approach, with a cut-off of $p = 0.05$. Depending on their availability at different time periods in the different registers, several variables contained a high number of missing values for neonatal characteristics because data collection of neonatal events in children with CP is always done retrospectively. It is likely that this missing information is not randomly distributed as the information is more likely to be recorded in cases with neonatal events and less so in those children born following an uneventful pregnancy and delivery. To address this, each of the univariate and multivariate analyses were repeated; the first excluded from the analysis all children with missing values whereas in the second analysis, a missing value was considered as the absence of event. As the results obtained by the two methods were similar, for simplicity only the results from the second analysis are presented.

In order to minimize findings that, due to high denominator figures were of statistical significance but of little clinical relevance, the threshold selected for analyzing trend in prevalence was $p < 0.005$ for overall prevalence. The threshold for other analyses was $p < 0.05$. Statistical analyses were performed using Stata Statistical software (version 10.0, Stata Corp., College Station, TX, USA).

Table 1 – Description of SCPE data on children with cerebral palsy included in the study.

	Years covered	Number of children with cerebral palsy born in the area covered by the register	Number of children with epilepsy N (%)
Grenoble, France	1980–1998	561	228 (40.6)
Toulouse, France	1976–1998	499	203 (40.7)
Edinburgh, UK	1984–1990	591	239 (40.4)
Cork, Ireland	1976–1998	346	140 (40.5)
Belfast, UK	1981–1998	1018	433 (42.5)
Göteborg, Sweden	1976–1998	1018	324 (31.8)
Dublin, Ireland	1976–1998	900	393 (43.7)
Newcastle, UK	1976–1998	923	305 (33.0)
Oxford, UK	1984–1998	1276	343 (26.9)
Copenhagen, Denmark	1976–1998	1601	448 (28.0)
Roma, Italy	1977–1998	191	89 (46.6)
Arnhem, Netherlands	1977–1988	126	51 (40.5)
Tönsberg, Norway	1991–1998	222	82 (36.9)
Bologna, Italy	1990–1996	77	34 (44.2)
Galway, Ireland	1990–1998	101	49 (48.5)
Madrid, Spain	1991–1998	86	24 (27.9)
Lisbon, Portugal	1996–1997	118	39 (33.0)
Total	1976–1998	9654	3424 (35.5)

3. Results

Of the 11725 children included in the database, 9654 from 17 registers were eligible for inclusion in the analyses (Fig. 1). This included 5268 children with BS-CP (54.5%), 2930 children with US-CP (30.3%), 694 children with dyskinetic CP (7.2%), 395 children with ataxic CP (4.1%) and 367 children with unclear or unknown subtype (3.8%). A history of epilepsy was reported in 3424 children (35%), the frequency varying between registers from 27 to 48% (Table 1). Seventy-two percent of children with epilepsy were on medication at time of registration.

The overall prevalence of CP associated with epilepsy was 0.69 per 1000 live births (99% CI 0.66—0.72). When analyzing trends in prevalence for the 15 registers with denominator data, there was a significant interaction between register and birthyear ($p < 0.001$). Changes in the prevalence rate over the period were not significant in 12 registers whereas the two French registers showed a linear decrease: −7.5% (95% CI −5.4 to −9.5%), $p < 0.001$ in Toulouse and −3.1% (95% CI −0.5 to-5.6%) in Grenoble, $p = 0.02$. In Newcastle, there was a significant linear increase of 2.5% (95% CI, 95% CI 0.3–4.6%, $p = 0.02$). Excluding the register with the greatest slope, i.e. Toulouse register, there was no longer a significant interaction and the overall prevalence between 1976 and 1998 followed a quadratic trend ($p < 0.001$ for the quadratic term), increasing over the period 1976–1983, and decreasing afterwards (Fig. 2). Considering time periods of five years (except for the last period of 3 years), the proportion of children with epilepsy among children with CP was highest in the period 1981–1985, i.e. 36.7% (34.4–39.0%) and the lowest in the last period 1995–1998, i.e. at 32.4% (30.0–35.0%). Although individually not significantly different from the period 1976–1980, the proportion with epilepsy showed a decrease over time (p test for trend = 0.06).

Among the 9654 children, 517 (5.4%) had CP of known postneonatal origin. The median age of postneonatal insult was 10 months (IQR, 3—22); only 20% of children had a postneonatal event after two years old. This group of children was at increased risk of developing epilepsy when compared with other children [314/517 (60.7%) vs. 3110/9137 (34.0%), $p < 0.001$].

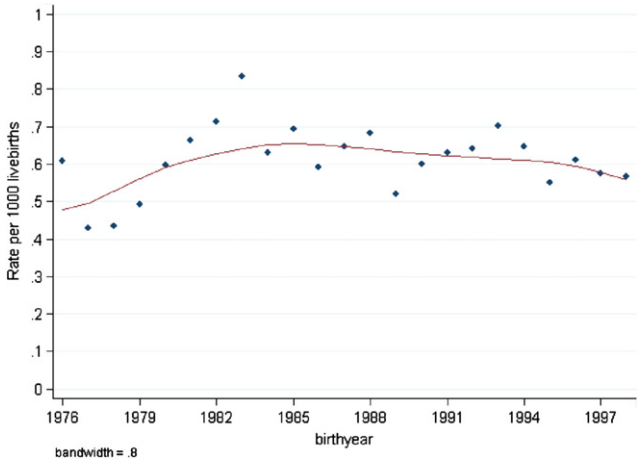

Fig. 2 – Smooth curve of prevalence of children with cerebral palsy and epilepsy in Europe between 1976 and 1998 (data from 16 registers).

Among the 9137 CP cases not known to be of postneonatal origin, eight out of 13 neonatal characteristics listed in Table 2 were associated with greater odds of epilepsy during infancy. The odds of epilepsy increased with increasing gestational age or birthweight. In the multilevel multivariable analysis (Table 3), characteristics independently associated with epilepsy in infancy were the presence of a brain malformation or a syndrome, a term or moderately preterm birth compared with a very premature birth, and signs of perinatal distress (neonatal seizures, neonatal ventilation and admission to NCU). The probability of epilepsy differed according to the type of brain malformation ($p < 0.001$), and was highest for children with microcephalus (65.0%) and lowest among children with a malformation coded as "other specified anomaly" (38.7%) including malformations such as schizencephaly or porencephaly. The following variables were not significant in the multivariable model: birthweight, multiple birth and Apgar score at 5 min. Among term children, ventilation, admission to NCU, neonatal seizures, and brain malformation were significantly associated with epilepsy, whereas among premature children, admission to NCU was not associated with epilepsy (Table 3).

The presence of epilepsy was associated with CP subtype, occurring more frequently in children with a dyskinetic (51.6%) or BS form (36.6%) (Table 4). In addition, severe intellectual impairment, sensory impairments and the inability to walk were associated with epilepsy. More than half of the children with epilepsy (i.e. 53.7%) were unable to walk in comparison with 18.3% of children without epilepsy. Children with US-CP were able to walk alone in 91% of cases, whereas only 35% of those with BS-CP could walk alone. Nevertheless, among children with US-CP, 22.8% of those able to walk alone had epilepsy (517/2267) versus 68.8% of those unable to walk (53/77). Among children with BS-CP, 15.9% of those able to walk alone had epilepsy versus 60.1% of those unable to walk. Thus, children with US-CP were at higher risk of having epilepsy than children with BS-CP when taking into account their ability to walk, associated impairments and gestational age (OR = 1.88, 95% CI 1.62–2.19, $p < 0.001$). Children with dyskinetic CP were more often born at term in comparison with spastic CP children (67% vs 41% for BS and 62% for US, $p < 0.001$). Moreover, neonatal seizures were more common among this group (29% vs 8% for BS and 5% for US, $p < 0.001$), they were more often hospitalized in a neonatal care unit at time of birth (42% vs 39% for BS and 27% for US, $p < 0.001$), and more often they had a recorded apgar score < 4 (5% vs 1% for BS and 0.3% for US, $p < 0.001$). At age of registration in registries, 36% of children with a dyskinetic form of CP were severely impaired (not able to walk even with aids and IQ<50), in comparison with 26% of BS and 2% of US, $p < 0.001$.

No significant correlations were observed between the proportion of children with epilepsy in a register and the proportion of children born at term, with the proportion of children with mild CP, with the proportion of children with a dyskinetic or a bilateral spastic form, nor with the proportion of children with a bilateral spastic CP and unable to walk.

Table 2 – Univariable analysis of epilepsy on neonatal characteristics in children with cerebral palsy ($n = 9137$), postneonatal cases excluded.

Variable, *n* (%)	N	Children with epilepsy, N (%)	OR (95% CI)	*p*
Sex				0.12
Female	3823	1336 (34.9)	1.0	
Male	5313	1773 (33.4)	0.93 (0.85–1.02)	
Gestational age				<0.001
<32 weeks	2184	522 (23.9)	1.0	
32–36 weeks	1627	483 (29.7)	1.34 (1.16–1.55)	
≥37 weeks	4661	1819 (39.0)	2.04 (1.81–2.29)	
Birth weight				<0.001
<1500 g	1801	437 (24.3)	1.0	
1500–2500 g	2112	630 (29.8)	1.33 (1.15–1.53)	
≥2500 g	4605	1777 (38.6)	1.96 (1.73–2.22)	
Small for gestational age				0.57
No	6969	2306 (33.1)	1.0	
Yes	1361	461 (33.9)	1.04 (0.92–1.17)	
Multiple birth				0.001
Singleton	7607	2598 (36.1)	1.0	
Multiple	831	236 (28.4)	0.76 (0.65–0.90)	
Mother's age, median [IQR]	5754	28 (24–32)	1.00 (0.99–1.01)	0.52
Parity				0.68
Non-primiparous	1965	706 (35.9)	1.0	
Primiparous	1881	664 (35.3)	1.03 (0.90–1.17)	
Apgar <4 at 5 min				<0.001
No	4220	1365 (32.3)	1.0	
Yes	97	53 (54.6)	2.52 (1.68–3.78)	
Neonatal seizures[a]				<0.001
No	3947	1216 (30.8)	1.0	
Yes	370	202 (54.6)	2.70 (2.17–3.36)	
Admission to a neonatal care unit				0.97
No	5993	2039 (34.0)	1.0	
Yes	3144	1071 (34.1)	1.00 (0.91–1.10)	
Neonatal ventilation				0.02
No	3713	1195 (32.2)	1.0	
Yes	604	223 (36.9)	1.23 (1.03–1.48)	
Syndrome				<0.001
No	8898	2995 (33.7)	1.0	
Yes	239	115 (48.1)	1.83 (1.41–2.37)	
Brain malformation[b]				<0.001
No	7397	2761 (32.6)	1.0	
Yes	667	349 (52.3)	2.39 (2.03–2.80)	
Type of brain malformation (ICD code)[c]				<0.001
Microcephalus (742.1)	137	89 (65.0)	4.03 (2.82–5.76)	
Reduction deformities of brain (742.2)	127	58 (45.7)	1.83 (1.28–2.60)	
Congenital hydrocephalus (742.3)	91	51 (56.0)	2.77 (1.83–4.21)	
Other specified anomaly of brain (742.4)	119	46 (38.7)	1.37 (0.94–1.99)	
Unspecified anomaly of brain (742.9)	193	105 (54.4)	2.59 (1.94–3.46)	

Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range; ICD, international classification of diseases.
a Neonatal seizure, neonatal ventilation and apgar have been collected since birthyear 1990.
b Two registers did not collect data about brain malformation ($n = 1073$).
c Reduction deformities of brain included microgyria, agenesis of part of brain, etc. Other specified anomaly of brain included schizencephaly, porencephaly, etc. Unspecified anomaly of brain included all brain malformation without any specification.

4. Discussion

This study is the largest published series focusing on epilepsy in children with CP. We found that 35% of children with CP had a history of epilepsy. Some neonatal factors doubled the risk of developing epilepsy. Children with epilepsy were at higher risk of suffering from associated impairments and of being unable to walk. The prevalence of children with CP and

epilepsy increased between 1976 and 1983 and decreased afterwards. This pattern mirrored that of the prevalence of CP during this time period.[15,21] The proportion of children with epilepsy among children with CP tended to decrease over the two decades, although not significantly, despite progress in neonatal care.

A population-based study including 139 children in Iceland showed a higher decrease in the proportion of children with CP and epilepsy over time, from 38% for children born in 1990–1996 to 15% for those born in 1997–2003.[22] The frequency of epilepsy in children with CP reported here is consistent with studies performed in other settings.[9,11,13] However, lower rates are reported when the definition is more restricted; e.g. seizures in the last 12 months were observed in 17% of children with CP in a population-based Canadian study.[14] The percentage of children on anti-epileptic medication in our study (72%) was similar to the proportion seen in other studies, who have reported percentages ranging between 75 and 95%.[9,10] Epilepsy is related to brain lesions and is consequently enduring. It also plays an important part in compromising the autonomy of adolescents and young adults.[23,24] Appropriate management and treatment of epilepsy are crucial to the care for children with CP.

Several neonatal characteristics were associated with a higher probability of epilepsy. Although neonatal seizures were a strong predictor of epilepsy in CP children, 45% of children with neonatal convulsions in this study did not go on to develop epilepsy. The association between gestational age or birthweight and epilepsy in children with CP is inconsistent between studies. Kulak et al.[9] showed that low birth weight was associated with increased risk of epilepsy whereas gestational age had no impact. Conversely, Zelnik et al.[13] reported that children born at term were at increased risk. Our results corroborate this last study as we found a OR of two of developing epilepsy for children born at term or ≥2500 g when compared with children born extremely preterm or of very low birthweight. This is likely to be related to the predominance of white matter lesions in preterm children,[25] as these are less likely to give rise to epilepsy than lesions of the grey matter, more usually seen in term children with CP.[26] The association between neonatal characteristics and epilepsy did not vary according to gestational age, with the exception of ventilation and admission to NCU that were not associated when the child was born preterm.

The frequency of epilepsy varied by CP subtype. When comparing and/or pooling data between several registers, SCPE collaborators chose to describe children as BS- or US-CP as there was considerable lack of reliability when children were described as having diplegic or tetraplegic spastic CP.[15,27] Using this classification, BS-CP is a large and heterogeneous group. In order to improve precision, this group can be subdivided, based on walking ability, as walking ability is less prone to coding variability between registers. In other studies,[1,3,13,28] children with spastic tetraplegia are those more at risk for epilepsy. In our study, we found that BS-CP children unable to walk (likely to be similar to tetraplegic CP) were much more likely to suffer from epilepsy than those able to walk (similar to diplegic CP with predominantly periventricular white matter lesion). Although children with US-CP were those with the lowest proportion of epilepsy (25.6%), after adjusting for walking ability and associated impairments, children with US-CP where at higher risk of developing epilepsy compared with BS-CP children. This is similar to reports from other studies, where children with hemiplegia (US-CP) were more at risk than those with diplegia (BS-CP able to walk).[9,13] This clinical finding reflects findings from imaging studies that show that deep grey matter lesions are more often seen in US-CP than in BS-CP.[29] Further, children with hemiplegia, those with perinatal arterial ischemic stroke seemed more at risk for epilepsy with a rate reaching 54% in a recent study.[30] About half of all children with dyskinetic CP had a history of epilepsy, higher than rates reported in two other population-based studies (7%[14] and 43%[3]), although this wide variation probably reflects the small number of cases with dyskinetic CP in these two studies. In hospital-based studies, rates of epilepsy in the dyskinetic group are higher, ranging between 25 and 56%.[11,13] However, in dyskinetic CP, it may be difficult to differentiate

Table 3 – Neonatal characteristics independently associated with epilepsy for all children with cerebral palsy ($n = 4147$) and stratified by gestational age, postneonatal cases excluded.[a]

Characteristics	All	<32 weeks, N = 1168	32–36 weeks, N = 758	≥37 weeks, N = 2221
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gestational age				
<32 weeks	1.0	–	–	–
32–36 weeks	1.34 (1.08—1.62)	–	–	–
≥37 weeks	2.23 (1.85—2.68)	–	–	–
Neonatal seizures	2.48 (1.91—3.22)	2.49 (1.34—4.61)	2.11 (1.05—4.22)	2.19 (1.56—3.06)
Ventilation	1.39 (1.09—1.77)	1.13 (0.80—1.62)	2.12 (1.30—3.46)	1.54 (1.02—2.31)
Admission to a neonatal care unit	1.32 (1.08—1.62)	0.76 (0.55—1.07)	1.07 (0.60—1.90)	1.57 (1.23—2.00)
Brain malformation	2.43 (1.91—3.08)	3.51 (1.82—6.78)	2.33 (1.31—4.15)	2.28 (1.71—3.03)
Syndrome[b]	1.73 (1.13—2.64)	1.49 (0.35—6.21)	2.26 (0.89—5.75)	1.57 (0.94—2.62)

Abbreviations: OR, odds ratio; CI, confidence interval.

a Data from 1990 to 1998.

b Syndromes were defined in accordance with Smith's book.[18]

Table 4 – Univariable analysis of epilepsy on cerebral palsy type and associated impairments ($n = 9137$).

Variable	N	Children with epilepsy, *n* (%)	OR (95% CI)	*p*
CP subtype				<0.001
Bilateral spastic	5062	1854 (36.6)	1.0	
Unilateral spastic	2699	691 (25.6)	0.60 (0.54–0.66)	
Dyskinetic	663	342 (51.6)	1.84 (1.57–2.17)	
Ataxic	367	100 (27.2)	0.65 (0.51–0.82)	
Bilateral spastic CP, able to walk alone	1663	265 (15.9)	1.0	<0.001
Able to walk with aids	1088	278 (25.5)	1.81 (1.50–2.19)	
Unable to walk	2029	1219 (60.1)	7.94 (6.65–9.48)	
Walking ability				<0.001
Alone	4456	905 (20.3)	1.0	
With aids	1500	447 (29.8)	1.67 (1.46–1.90)	
Unable even with aids	2601	1570 (60.4)	5.98 (5.31–6.72)	
Severe intellectual impairment				<0.001
No	5833	1139 (19.5)	1.0	
Yes	2265	1535 (67.8)	8.67 (7.66–9.80)	
Severe visual impairment				<0.001
No	8198	2415 (29.5)	1.0	
Yes	939	695 (74.0)	6.82 (5.81–8.00)	
Severe hearing impairment				<0.001
No	8941	3015 (33.7)	1.0	
Yes	196	95 (48.5)	1.85 (1.39–2.46)	

Abbreviations: OR, odds ratio; CI, confidence interval; CP, cerebral palsy.

partial complex seizures from dyskinetic movements potentially resulting in over- as well as under diagnosis of epilepsy.[2] Furthermore, the higher rate of epilepsy reported within the dyskinetic group may relate to the definitions used to classify dyskinetic CP. Several authors have described a mixed CP type, mainly spastic and dyskinetic, whereas SCPE group classifies children according to the predominant clinical features.[31] In addition, children with dyskinetic CP more often had additional, neonatal risk factors for epilepsy than children presenting with other types of CP, and this too could contribute to the findings. Children with pure dyskinetic subtype usually have a basal ganglion lesion and are unlikely to have epilepsy, unless they also have a cortical lesion. The later can be observed in term babies for example, suffering from acute hypoxia or anoxia damaging not only in the basal ganglia but also in the rolandic, highly epileptogenic, areas.

Children with intellectual, visual and hearing impairment were at increased risk of epilepsy, most probably related to the severity of their brain lesions. The association between epilepsy and mental retardation has been widely described. Whether epilepsy is the cause of a low IQ in CP or an indicator of more widespread injury resulting in both epilepsy and a low IQ is impossible to disentangle from this study. CP arises from a cerebral lesion, including cortical lesions, some of which are highly epileptogenic, for example those in the temporal and frontal lobes; a refractory epilepsy always worsens the cognitive (and frequently also the motor) prognosis in CP. The association with hearing and visual impairment has been less well examined[11] but this is likely to be explained by the fact that cortical lesions lead to different manifestations. When a standardized description for neonatal ultrasound and magnetic resonance imaging results is available, it should be possible to study in greater detail the association between the type of cerebral lesion and epilepsy.

Our study has several strengths. It is the first study to estimate prevalence rate of children with CP and epilepsy as well as trends in percentages of children with epilepsy over a long period. It is a large population-based study, covering a wide geographical area, and therefore, unlike in smaller studies, the children are more likely to be representative of the population of children with CP. All registers participating in SCPE network use the agreed definitions for all characteristics in the common database, including the definition for epilepsy.

There are several reasons that might contribute to the observed wide variation in epilepsy rates between countries seen in our study. First, the older a child is at time of registration, the less likely it is that the diagnosis of epilepsy is missed. In our study population, the median age at registration was 6.5 years old (interquartile range 5.0–8.1). Although some children may have developed epilepsy after this age, this is likely to be only a small number, as between 47 and 79% of CP children with epilepsy have seizures in the first years of life.[11,12,28] Moreover, in our database, there was no linear relationship between median age of registration in a register and percentage of cases with epilepsy in the register. Second, some of the variation in the rates of epilepsy could be explained by differences in perinatal or clinical factors across registers. Although we did not find any association between the characteristics about which we collected data, we cannot exclude the possibility that unreported characteristics could contribute to the findings. Third, the accuracy of diagnosis of epilepsy might be prone to variation between registers or over time. Indeed, this study covered a period of 22 years, with different diagnostic tools for epilepsy in use in the late seventies as compared with the late nineties. A previous study

showed that a false diagnosis of epilepsy could affect up to 30% of children.[32] As in many studies, in our study we relied on clinical records to indicate if a child has epilepsy. More detailed information on treatment type (e.g. mono or polytherapy) would have been informative, but it was not feasible for most of the registers to collect this level of detail. The lack of a consensual scale to describe epilepsy severity precludes stratification at this level. Despite these limitations around the accuracy of diagnosis of epilepsy, this epidemiological study remains the largest study to date, covering a wide population, and enables us to describe the prevalence and risk factors for epilepsy among children with CP.

5. Conclusion

Epilepsy among children with CP is common and the prevalence rate for children born in 1976–1998 mirrored that of the prevalence of CP. The observed relationship between epilepsy and associated impairments was as predicted. However, it requires longitudinal studies of children with CP and epilepsy to further improve our understanding of the relationship between epilepsy and CP and of the impact of having both on those so affected.

REFERENCES

1. Wallace SJ. Epilepsy in cerebral palsy. *Dev Med Child Neurol* 2001;**43**:713–7.
2. Ashwal S, Russman BS, Blasco PA, et al. Practice parameter: diagnostic assessment of the child with cerebral palsy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology* 2004;**62**:851–63.
3. Carlsson M, Hagberg G, Olsson I. Clinical and aetiological aspects of epilepsy in children with cerebral palsy. *Dev Med Child Neurol* 2003;**45**:371–6.
4. Vargha-Khadem F, Isaacs E, van der Werf S, Robb S, Wilson J. Development of intelligence and memory in children with hemiplegic cerebral palsy. The deleterious consequences of early seizures. *Brain* 1992;**115**(Pt 1):315–29.
5. Beckung E, Hagberg G, Uldall P, Cans C. Probability of walking in children with cerebral palsy in Europe. *Pediatrics* 2008;**121**: 187–92.
6. McLellan A. Epilepsy – an additional risk factor for psychological problems in cerebral palsy. *Dev Med Child Neurol* 2008;**50**:727.
7. Carlsson M, Olsson I, Hagberg G, Beckung E. Behaviour in children with cerebral palsy with and without epilepsy. *Dev Med Child Neurol* 2008;**50**:784–9.
8. Hammal D, Jarvis SN, Colver AF. Participation of children with cerebral palsy is influenced by where they live. *Dev Med Child Neurol* 2004;**46**:292–8.
9. Kulak W, Sobaniec W. Risk factors and prognosis of epilepsy in children with cerebral palsy in north-eastern Poland. *Brain Dev* 2003;**25**:499–506.
10. Hadjipanayis A, Hadjichristodoulou C, Youroukos S. Epilepsy in patients with cerebral palsy. *Dev Med Child Neurol* 1997;**39**: 659–63.
11. Zafeiriou DI, Kontopoulos EE, Tsikoulas I. Characteristics and prognosis of epilepsy in children with cerebral palsy. *J Child Neurol* 1999;**14**:289–94.
12. Gururaj AK, Sztriha L, Bener A, Dawodu A, Eapen V. Epilepsy in children with cerebral palsy. *Seizure* 2003;**12**:110–4.
13. Zelnik N, Konopnicki M, Bennett-Back O, Castel-Deutsch T, Tirosh E. Risk factors for epilepsy in children with cerebral palsy. *Eur J Paediatr Neurol* 2010;**14**:67–72.
14. Shevell MI, Dagenais L, Hall N. Comorbidities in cerebral palsy and their relationship to neurologic subtype and GMFCS level. *Neurology* 2009;**72**:2090–6.
15. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Surveillance of Cerebral Palsy in Europe (SCPE). *Dev Med Child Neurol* 2000;**42**:816–24.
16. Prevalence and characteristics of children with cerebral palsy in Europe. *Dev Med Child Neurol* 2002;**44**:633–40.
17. Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Rognosis, International League Against Epilepsy. *Epilepsia* 1993;**34**:592–6.
18. Jones KL, editor. *Smith's recognisable patterns of human malformation*. 5th ed. 1997.
19. Marsal K, Persson PH, Larsen T, et al. Intrauterine growth curves based on ultrasonically estimated foetal weights. *Acta Paediatr* 1996;**85**:843–8.
20. Gardosi J, Mongelli M, Wilcox M, Chang A. An adjustable fetal weight standard. *Ultrasound Obstet Gynecol* 1995;**6**:168–74.
21. Blair E, Watson L. Epidemiology of cerebral palsy. *Semin Fetal Neonatal Med* 2006;**11**:117–25.
22. Sigurdardottir S, Thorkelsson T, Halldorsdottir M, Thorarensen O, Vik T. Trends in prevalence and characteristics of cerebral palsy among Icelandic children born 1990 to 2003. *Dev Med Child Neurol* 2009;**51**:356–63.
23. Michelsen SI, Uldall P, Kejs AM, Madsen M. Education and employment prospects in cerebral palsy. *Dev Med Child Neurol* 2005;**47**:511–7.
24. Michelsen SI, Uldall P, Hansen T, Madsen M. Social integration of adults with cerebral palsy. *Dev Med Child Neurol* 2006;**48**:643–9.
25. Towsley K, Shevell MI, Dagenais L. Population-based study of neuroimaging findings in children with cerebral palsy. *Eur J Paediatr Neurol* 2011;**15**:29–35.
26. Krageloh-Mann I, Horber V. The role of magnetic resonance imaging in elucidating the pathogenesis of cerebral palsy: a systematic review. *Dev Med Child Neurol* 2007;**49**:144–51.
27. Colver AF, Sethumadhavan T. The term diplegia should be abandoned. *Arch Dis Child* 2003;**88**:286–90.
28. Kwong KL, Wong SN, So KT. Epilepsy in children with cerebral palsy. *Pediatr Neurol* 1998;**19**:31–6.
29. Krageloh-Mann I, Cans C. Cerebral palsy update. *Brain Dev* 2009;**31**:537–44.
30. Wanigasinghe J, Reid SM, Mackay MT, et al. Epilepsy in hemiplegic cerebral palsy due to perinatal arterial ischaemic stroke. Dev Med Child Neurol;52:1021-1027
31. Himmelmann K. Hands-on in cerebral palsy research. *Dev Med Child Neurol* 2009;**51**:497–8.
32. Uldall P, Alving J, Hansen LK, Kibaek M, Buchholt J. The misdiagnosis of epilepsy in children admitted to a tertiary epilepsy centre with paroxysmal events. *Arch Dis Child* 2006; **91**:219–21.